ABSTRACT

Objective: The pre- and postoperative care for fractionated laser resurfacing is still controversial, especially in regard to the use of antibiotics to prevent bacterial infection and potential consequences. Recently, an ionic hydrogel has shown to be useful in the postoperative treatment of minor burns. The aim of this study is to evaluate the use of this hydrogel after fractional laser treatments targeting photoaging and chronoaging damage to skin. **Design:** A randomized prospective study. **Setting:** one plastic surgeon private practice. **Participant:** Fifty patients with chronoaging and photoaging cosmetic issues were enrolled in two different post-treatment regimens: ionic hydrogel alone and ionic hydrogel in combination with antibiotics. **Measurements:** Patients were evaluated for healing time, complications, and postoperative pain, the latter assessed with a 10-point visual analogue score. A questionnaire to investigate how patients managed through the postoperative phase was also provided to each patient. **Results:** No significant differences between the two groups were observed in regard to

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ORIGINAL RESEARCH

Ionic Hydrogel Monotherapy and in Combination with Antiviral-Antibiotic Prophylaxis, in the Post-procedure Management of Fractional Laser-Treated Patients

FRANCESCA ROMANA GRIPPAUDO, MD, PhD
Assistant Professor in Plastic Surgery, NESMOS Dept., Sapienza University of Roma, Roma, Italy

FRACTIONAL LASER resurfacing (FLR) has shown to yield excellent results for several skin diseases, and with minimal side effects,[1–3] thereby combining the advantages of ablative and nonablative laser resurfacing. There is strong, level-B evidence of the efficacy and safety of FLR in photoaging, periorbital wrinkling, and acne scarring, making it a mainstay of the treatments available for these conditions.[4] Weaker, level-C evidence has also been shown for the treatment of other aesthetic conditions, such as post-burn and surgical scars, melasma, stretch marks, postinflammatory pigmentation, and nonaesthetic conditions, such as residual hemangiomas, telangiectatic matting, and superficial disseminated actinic porokeratosis.[4] The concept FLR is based on is quite simple. FLR delivers a laser beam that is divided into columns of treatment at various depths into the skin. These columns are known as microthermal zones (MTZs)—once the columns are

Disclosure: Dr Grippaudo received Procutase® Hydrogel for use in this work from ICIM, Milano, Italy.

Author correspondence: Francesca Romana Grippaudo, MD, PhD; E-mail: frgrip@hotmail.com

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healing time, postoperative pain, complications, and patient satisfaction. **Conclusion:** Ionic hydrogel alone has shown to provide adequate skin care support in the postoperative phase of fractional-laser-resurfacing-treated patients.

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delivered, the surrounding 'normal' skin triggers its chemotactic and wound-healing properties, which leads to tissue contraction, stimulation of collagen, and rapid wound healing.

A number of post-FLR potential complications and side effects have been described in the literature, including transient and persistent erythema; pruritus; milia and acneiform eruptions; bacterial, candidal or viral infections; contact dermatitis; hyper- or hypopigmentation; and scarring.[1,3] In order to avoid these side effects, a wide variety of topical cosmetic products has been suggested for post-treatment phases, including vitamins A, C, E, and K and growth factors (neocollagen synthesis, fibroblast activation, wound-healing enhancement, photoprotection, anti-inflammatory action) as well as pre-treatment aids based on skin-lightening agents (hydroquinone, azelaic acid, or kojic acid).[5] Re-epithelialization agents and moist dressings showed efficacy in promoting skin repair, as would occur with a partial-thickness burn wound that must heal by keratinocyte migration from cutaneous appendages.[5]

Nonunivocal protocols and results have shown that FLR-related pre- and postoperative care remains a controversial issue, especially in regard to the use of antibiotics to prevent bacterial infection and the potential consequences.

The literature reports an infection rate ranging from six to eight percent of all patients treated with ablative resurfacing devices, which has led to recommending the implementation of antiviral and antibacterial prophylactic measures[2] and related guidelines. Such protocols suggest, for instance, the use of cefixime, dicloxacillin, azithromycin or clarithromycin,[1,6–8] and acyclovir, with various administration-time schemes.

Recently, an ionic hydrogel (Procutase® [ICIM, via Peloritana 28, 20024, Garbagnate Milanese, Milano, Italy]) has shown to be useful in the management of non-complicated, minor, outpatient burns (total body surface area <10% and no deeper than superficial 2nd degree burns).[9] This product is a hydrogel composed of natural hydrophilic polymers in an active ionic solution with trace metals and with an inhibitor of matrix metalloproteinases MMP-1, -3, and -9 (collagenase/gelatinase). The aim of this study is to evaluate the use of ionic hydrogel, applied alone or combined with antibiotics, as postoperative care in patients treated with FLR for photoaging and chronoaging skin damage.

METHODS

From March 2013 to October 2014, 50 patients seeking medical care for aesthetic concerns, including skin laxity, photodamage, skin dyschromias, and wrinkles, were enrolled in the study and treated by the author of this article in a private practice. Inclusion criteria included healthy male and female individuals

between the ages of 38 and 68 years (mean age: 53 years). Patients with moderate photodamage, with a baseline Fitzpatrick Wrinkle and Elastosis Score of 2 to 6 and with Fitzpatrick skin types II to V were selected for inclusion in the trial.

Exclusion criteria included pregnancy or breastfeeding, history of abnormal photosensitivity with possible hyperpigmentation, hypertrophic/keloid scar formation tendency, recent use of ultraviolet lamps or self-tanning lotions, presence of inflammation, history of herpes simplex virus 1, use of isotretinoin or retinoids in the past year, having had a chemical peel or dermabrasion within three months of the clinical trial start date, having had nonablative laser resurfacing or other light-based procedures performed in the treatment areas within six months prior to enrolment into the clinical trial, use of botulinum toxin A in the face within six months of the clinical trial start date, having had any surgical procedure in the face within 12 months of the clinical trial start date, a history of autoimmune or immunosuppressive disorders, and any history of skin cancer in the treatment areas.

Two patients with a history of filler treatments but with no records of previous treatment underwent high-frequency ultrasound (HFUS) for evaluation according to the already described protocol[10,12]—both received laser treatment, yet avoided the periorbital area, where some filler material had been detected. Thirty-six patients had already undergone aesthetic medicine or surgery procedures in the past.

A systematic, customized, written informed consent was obtained from every patient, making sure that all patients received clear, proper information on the treatment and the treatment schedule. All treatments were performed using a fractionated CO_2 laser, 10,600nm wavelength, continuous superpulse, with microscanner for fractionated treatment (AcuPulse™ MultiMode™ SuperPulse™, Lumenis INC, Santa Clara, California).

Settings were condition-specific. For dyschromia, laser was set to superficial mode, pulse energy 70 to 100mJ, density 40–60% spot diameter 1.3mm; for wrinkles, laser was set to deep mode, pulse energy 10 to 20mJ, density 10–20% spot diameter 0.12mm. The average duration of each treatment was 30 minutes.

All of the patients were given antiviral prophylaxis with 400mg acyclovir tablets every eight hours to be started one day prior to the procedure and continued up to post-treatment Day 5. Patients were instructed to come for treatment on an empty stomach and with a helper to assist them. Male patients had to be shaved. All patients had to remove any contact lenses and wear regular glasses, if needed.Upon patient's arrival for the treatment, skin was washed with a specific soap, then prepped with a 70% alcohol disinfectant and rinsed with sterile saline. Patients received FLR after a one-hour occlusive application of a topical anesthetic cream (lidocaine 15%, prilocaine 5%), which was then removed just before treatment.

Following FLR treatment, patients were randomly divided in two groups (A and B), which were homogenous in age, Fitzpatrick skin type, and Fitzpatrick wrinkle score. Group A patients (25) were treated with cold saline gauzes for relief and inflammation control, ionic hydrogel was then applied on the entire treated area (Figure 1) as a temporary wound dressing with sterile gauze and supporting mesh to be left on until the patients reached home.

Patients were instructed to perform self-medication at home and, specifically, to carefully remove the gauze once at home, wash skin with a gentle cleanser, rinse with sterile saline, and apply ionic hydrogel twice a day. The patients were also told to avoid sun exposure and apply sun protection factor (SPF) 50+, to not scratch or remove any scabs that might have formed, to use a very gentle cleanser, avoid swimming and other sports involving physical contact for seven days after the treatment, use corticosteroids for the periocular region, and to sleep on two pillows.

Group B patients (25) were treated with the same Group A protocol, but they also underwent standard antibiotic prophylaxis with 250mg clarithromycin taken orally twice a day for five days.

All Group A and Group B

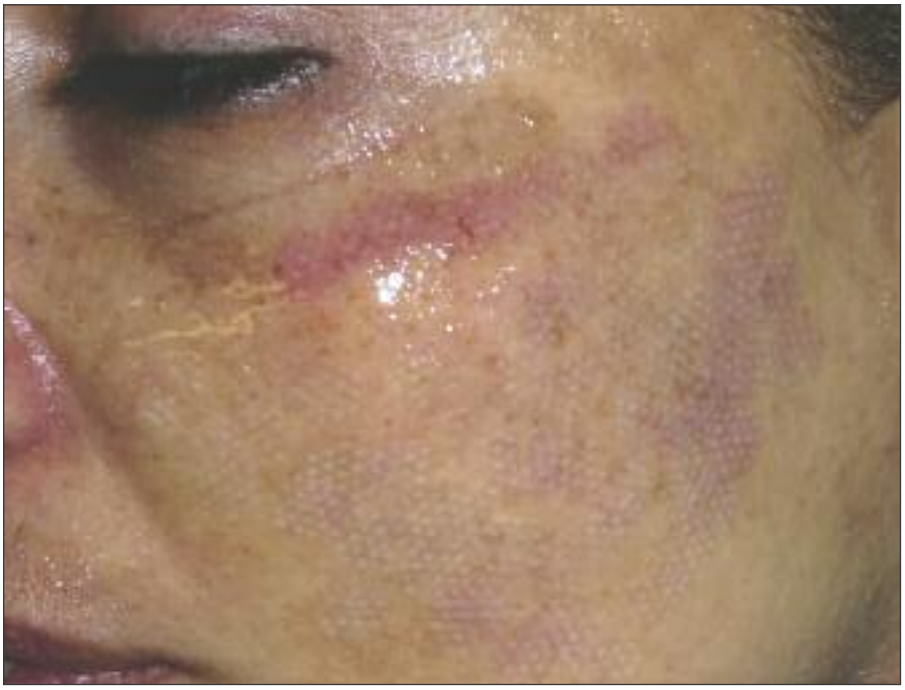

Figure 1. Skin appearance immediately after fractional laser procedure for facial dyschromias. Ionic hydrogel has been applied over treated area.

patients were seen at post-procedure Day 5 for re-evaluation, and then every three days until full healing. Healing time was evaluated based on the time the crusts that typically appear after treatment needed to disappear. The degree of photoaging and the efficacy of treatment were evaluated using a five-point scale based on the assessment of fine lines, mottled pigmentation, tactile roughness, and coarse wrinkles, yet these will not be discussed in this paper. Pain levels were assessed for all patients during treatment and for 25 minutes after treatment was completed. Pain was assessed using a 10-point visual analogue scale (VAS) in which 0 is no pain and 10 is intolerable pain. When patients returned for follow-up one month after the treatment, they received a questionnaire to fill out to investigate how well they managed through the postoperative phase, thus assessing patient adherence.

Statistical analysis on retrieved data was conducted with a Student's t-test, with a significance level of $p<0.05$.

RESULTS

All Group A patients completed the clinical evaluation, while two Group B patients dropped out of the protocol at post-procedure Day 3 because of antibiotic intolerance. There was no difference between the two groups (ionic hydrogel + clarithromycin vs. ionic hydrogel alone) in regard to infection rates, with actually no infection or delayed healing reported. No herpes outbreaks were reported.

During the first week, pruritus occurred in 22 patients (8 Group A patients, 14 Group B patients). It was either self-limited or controlled by antihistamines. In 11 patients (5 Group A patients, 6 Group B patients), a sensation of discomfort was observed in the first week and alleviated by the use of paracetamol 1000mg tablets. No dyspigmentation, dermatitis or scarring was observed in the two groups. Downtime healing times were completely comparable between the two groups.

The mean pain level during treatment was 3.9 in Group A patients and 4.0 in Group B patients, according to the VAS pain scale. The burning sensation, assessed 20 minutes after the treatment was 4.8 for both Groups. No patient reported any pain after 20 minutes.

The mean healing time (measured as the time between treatment completion and the resolution of the crusting) was 5.1 days in Group A patients and 5.0 in Group B patients. All the mean values have $p>0.05$ and show no statistical differences between the two groups. Interestingly, Group A patients showed much better adherence to the protocol and reported being glad they were not forced to undergo any antimicrobial prophylaxis.

DISCUSSION

Fractional laser treatments have become a mainstay in the

treatment of a variety of skin conditions. FLR has been used to treat photodamaged skin, benign hyperpigmentation, and scars. The potential complications related to these treatments are well-outlined in the literature and include transient and persistent erythema; pruritus; milia or acneiform eruption; contact dermatitis; hyper- or hypo-pigmentation and scarring; and bacterial, mycotic, or viral infection.[1]

Infection after laser resurfacing is of primary concern because the epidermis and part of the dermis are removed, which increases the risk of infection. Infections with *Staphylococcus aureus* or *Pseudomonas aeruginosa* may occur,[13] usually appearing as pustules or yellow crusting, patchy erythema, or delayed healing with pain or pruritus. The risk of bacterial infections is minimized by the prophylactic use of systemic antibiotics and appropriate topical care. However, despite the many articles about antibiotic prophylaxis in laser resurfacing, there is still much controversy and disagreement. This has been further demonstrated in two recent papers in which experienced laser operators express opposing viewpoints on antibiotic prophylaxis.[14–16]

Pretreatment antiviral and antibiotic prophylaxis is generally still administered because of these nonunivocal protocols and as a form of defensive medicine.[17]

Infection after fractional laser treatment is uncommon, with scattered reports of few cases,[18–20] and an overall complication rate of 0.1 to 0.2 percent as reported after large series of FLR reviews.[16,21]

Recently, Procutase® has emerged as an advanced product for the treatment of skin lesions. Its formulation, based on a patented solution of ionized trace metals and plant-derived peptides, can help to control the moist microenvironment of the wound and create the ideal local conditions to enable quicker recovery and optimal cleansing of the wound bed. All of these properties make this hydrogel also recommended as an adjuvant for all those skin lesions where healing needs to be facilitated, such as wounds, ulcers, scalds, and burns.[9] Because of its properties, the author has started to use it in the postoperative care of FLR in a private practice environment, either associated with antibiotics or alone. The results demonstrated in this paper have confirmed the author's opinion that treated skin areas can be managed with ionic hydrogel as minor, superficial burns, leaving costly antimicrobial medication for selected patients only and, most importantly, for the first-line treatment of complications.

Furthermore, in order to achieve the best satisfaction of both the patient and the physician, and reduce the risk of having unhappy patients and possible litigations, especially common in the cosmetic field,[17] cosmetic surgeons need to carefully select patients through an accurate analysis of their medical history to identify possible risk factors or contraindications, provide adequate and realistic information to the patients on the number of treatment sessions required for every condition and the results to expect, and explain the possible complications or undesired effects.

Patients must be informed and instructed properly to fully understand and comply with the treatment plan offered. Full information should also be provided to allow patients to perform proper pre- and post-treatment self-care.

CONCLUSION

Similarly to the promising results achieved in the outpatient management of minor skin burns in a previous trial, ionic hydrogel alone has shown to provide adequate skin care support during the delicate healing days that follow FLR treatment, thus offering a treatment option for patients at low risk of developing complications.

Constant support by the physician and his or her staff is crucial to readily identify and treat every wound possibly prone to developing infection with appropriate antibiotic therapy.

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